REMARKS

A. Restriction Requirement

Applicant gratefully acknowledges rejoinder of Groups I and II of the Restriction Requirement mailed October 11, 2006. Accordingly, claims 19-36 are withdrawn from further consideration as being drawn to nonelected inventions.

Applicant respectfully points out that claims 25-34 recite methods of use for the specificity-determining substrate recited in claim 1. Therefore upon a finding of allowability of claim 1, Applicant respectfully requests rejoinder and examination of claims 25-34 in the proceedings of the instant application.

Applicant further confirms the election of succinyl as the specificity determining ligand in claims 2 and 11, and of silica as the support in claims 5 and 14.

In view of the election of succinyl as the specificity-determining ligand Applicant withdraws claims 3 and 12 from consideration as being drawn to a nonelected invention. Accordingly claims 1,2, 4-11, and 13-18 are currently subject to examination. Applicant reserves the right to prosecute the subject matter of all nonelected inventions in subsequent patent applications.

B. Amendments to the Claims

The amendment to claim 1 reciting "suitable for proteomic separations" is supported throughout the specification, and in particular at least at page 1, in the section Field of the Invention; page 3, 2nd paragraph; and page 11, 5th paragraph of text.

The amendment to claim 1 reciting "wherein the predetermined minimum distance is greater than about 5 Å" is supported in the specification at least at page 12, 3rd paragraph.

No new matter is introduced in the amendments to the claims.

ARGUMENT

A. Claims 1,2, 4-11, and 13-18 are patentable under 35 U.S.C. 112, 2nd paragraph.

The Office Action cites the word "predetermined" as lacking a clear definition in the specification. As part of this rejection the Office Action erroneously states that paragraph 0081 of the specification provides numbers such as "4" for the minimum distance, but that no units are

given (page 3, 7th paragraph of text). Applicant respectfully points out that in the specification as filed each number in the indicated paragraph is followed by the symbol "Å" (meaning Angstrom units, or 0.1 nm). The same symbols "Å" appear on the USPTO web site providing the electronic version of Published Patent Application 20040106131 for this application in the TIFF image pages. Thus the Office Action is mistaken in stating that no units are provided for the numbers. (Applicant has noted that in the html version of the same Patent Application Publication the symbols "Å" are missing; this may be the source of the error.) In view of Applicant's perfecting of the view of the specification, Applicant declares that the meaning of "predetermined minimum distance" is provided in the specification as filed.

Nevertheless Applicant has amended claim 1 to recite that the predetermined minimum distance is greater than about 5 Å. Accordingly Applicant submits that claim 1 as amended particularly points out and distinctly claims the subject matter which Applicant regards as the invention.

The Office Action rejects claims 6 and 15 for indefiniteness in reciting "a predetermined maximum content" but lacking clear definition as to the meaning of "predetermined" in the specification. Applicant respectfully points out that the specification, at page 12, 2nd paragraph (paragraph 0080) provides an extensive definition of the phrase "predetermined maximum content". Thus Applicant submits that claims 6 and 15 are clear, and that they particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

For these reasons Applicant respectfully submits that claims 1,2, 4-11, and 13-18 satisfy the requirements of 35 U.S.C. 112, 2nd paragraph, and requests that this rejection be withdrawn at this time.

B. Claims 1, 2, 4-6, 10, 11, and 13-15 are novel under 35 U.S.C. 102(b) as not anticipated by Keyes (U. S. Patent 4,714,676).

The present invention provides a specificity-determining substrate suitable for proteomic separations, wherein the specificity-determining substrate includes a specificity-determining ligand bound to a support wherein the spatial separation between adjacent ligand groups is greater than a predetermined minimum distance of about 5 Å (claim 1). The specificity-determining substrate forms a complex with a protein molecule in a homogenous fashion. Thus, in this invention, a specificity-determining ligand is linked to a support. Among the specificity-

determining ligands set forth in claim 2, Applicant has elected the succinyl group as the species subject to examination at this time. Thus according to claim 2, a succinyl group is bound to a substrate. The specificity-determining substrate that includes the succinyl-substrate combination has the property that it forms a complex with a protein molecule in a homogeneous fashion.

The present invention further provides a complex that includes a specificity-determining substrate as described in the preceding paragraph and a protein molecule (claim 10). In particular, the complex includes a protein molecule and a specificity-determining substrate that forms a complex with a protein molecule in a homogenous fashion. Thus, in this invention, a specificity-determining ligand that is elected as succinyl is linked to the support. Applicant emphasizes that in the complex, the specificity-determining ligand (succinyl) is bound to the support, and not to the protein moiety.

Keyes relates broadly to a naturally occuring protein that is chemically modified to provide the protein with activity of a selected enzyme (see Abstract). Keyes elaborates that a native protein is partially denatured in the presence of an inhibitor for the predetermined model enzyme, whose activity is to be modeled. Next, the partially denatured native protein, in the presence of the inhibitor of the model enzyme, is deposited on a solid support and cross-linked to define a new enzyme-like modified protein conformation which is defined by the inhibitor of the model enzyme and is preserved in an immobilized fashion on a solid carrier or support. (see Summary of the Invention) In an embodiment, Keyes discloses that a native protein may be reacted with succinic anhydride, at low pH, for example about pH 4, to produce new negatively charged carboxylic acid sites on the protein. The carboxylic acid sites which are produced by succinic anhydride reaction are formed by the reaction of the anhydride function on the succinic anhydride with free amine groups on the protein. Applicant emphasizes that in this instance it is the protein that is reacted with succinic anhydride.

Accordingly Applicant points out that Keyes fails to provide a specificity-determining substrate, wherein the specificity-determining substrate includes a specificity-determining ligand bound to a support (claim 1), and further fails to provide a complex that includes a specificity-determining substrate as described in the instant invention and a protein molecule (claim 10). In particular, Applicant emphasizes that Keyes, in an embodiment, reacts a **protein** with succinic anhydride to provide carboxyl groups bound to the protein, whereas the present invention, in the species elected for examination at this time, provides a **substrate** bound to a succinyl group. On

the basis of this fundamental distinction, Keyes fails to anticipate claims 1, 2, 4-6, 10, 11, and 13-15.

C. Claims 1, 2, 3-6, 8-11, 13-15, and 17-18 are novel under 35 U.S.C. 102(b) as not anticipated by Comb et al. (U. S. Patent 5,834,247).

Comb et al. relates broadly to modified proteins comprising an intervening protein sequence (IVPS) and a target protein, the IVPS being capable of excision by protein splicing, or cleavage in the absence of splicing, under predetermined conditions. (See Summary of the Invention) Comb et al. provides numerous modalities for preparing such modified proteins using combinations of recombinant DNA techniques and protein chemistry techniques (See Summary of the Invention)

Applicant respectfully points out that Comb et al. fails to provide a specificity-determining substrate suitable for proteomic separations, wherein the spatial separation between adjacent ligand groups bound to a substrate is greater than a predetermined minimum distance, of about 5 Å. The Office Action cites Fig. 28 as teaching a chitin binding column for the purification of expressed proteins fused with an intein and chitin binding domain (page 5, 4th paragraph). Applicant has scrutinized Fig. 28 as well as the legend to Fig. 28 in the Brief Description of the Drawings, and notes with all due respect that no disclosure related to Fig. 28 refers to a chitin binding column. Furthermore, any citation of a chitin column for binding to a chitin binding domain of a multicomponent fusion protein as depicted in Fig. 28 does not provide a specificity-determining substrate that binds native proteins suitable for proteomic separations. Thus this citation to Comb et al. in the Office Action is inapposite.

The Office Action cites cols. 57-58 as teaching preparations of substrates, including chitosan bound to Sepharose and chitin itself (page 5, 6th paragraph). The Office Action also cites Fig. 28 for disclosing a chitin ligand. These are cited as providing an "oligosaccharide" of claim 2. Applicant respectfully points out that in view of its election of succinyl as the specificity-determining ligand, other such ligands are not subject to examination at the present time. Applicant respectfully requests that this ground of rejection be held in abeyance until such time as an oligosaccharide is subject to examination.

The Office Action cites Sepharose modified by 1,4-butanediol diglycidoxy ether as a ground for rejection of claims 3 and 12. These claims are currently withdrawn from consideration as drawn to a nonelected invention. Thus the rejection of these claims is moot.

The Office Action cites a bead in Comb et al. as anticipating claims 5 and 14. Applicant respectfully points out that a bead is not an elected species currently under examination.

The Office Action cites a polysaccharide in Comb et al. as anticipating claims 8 and 17. Applicant respectfully points out that a polysaccharide is not an elected species currently under examination.

The Office Action cites chitosan in Comb et al. as anticipating claims 9 and 18. Applicant respectfully points out that chitosan is not an elected species currently under examination.

For these reasons Comb et al. does not anticipate the elected species of claims 1, 2, 3-6, 8-11, 13-15, and 17-18. Accordingly Applicant respectfully requests that this rejection be withdrawn at this time.

D. Claims 1, 2, 4-11, and 13-18 are nonobvious under 35 U.S.C. 103(a) over Comb et al. in view of Margel (U. S. Patent 4,732,811).

The Office Action has rejected all of claims 1, 2, 4-11, and 13-18 now subject to examination for obviousness over Comb et al. in view of Margel (page 6, 7th paragraph of text), even though the substance of the obviousness rejection is directed to the purported prima facie obviousness of only claims 7 and 16 (Office Action, pages 6-7).

In the absence of substantive grounds of rejection for obviousness of claims 1, 2, 4-6, 8-11, 13-15, and 17-18, Applicant considers these claims to be nonobvious under 35 U.S.C. 103(a) on their face. Furthermore, Applicant has clearly pointed out the deficiencies of Comb et al. above. Margel fails to remedy these deficiencies. Therefore Applicant respectfully submits that claims 1, 2, 4-6, 8-11, 13-15, and 17-18 are patentable under 35 U.S.C. 103(a) over the prior art of record, and request that the rejection of these claims be withdrawn at this time.

Margel relates generally to agarose and agar polyaldehyde beads, and processes for the synthesis of such beads. The polyaldehyde compounds e.g. polyacrolein, polymethacrolein or polyglutaraldehyde, are used as microspheres or as powders (see Abstract).

Claims 7 and 16 are dependent claims that recite the specificity-determining substrate of the invention, or the complex of the invention, respectively, wherein the solids content of the support when equilibrated with an ambient fluid is less than about 8% w/v. It is emphasized that this recitation relates to the proportion of solids within the volume occupied by a substrate composition in equilibrium with its ambient fluid medium. This is distinct from the interpretation in the Office Action that misrepresents the recitation as being the solids content of any slurry or suspension of the specificity-determining substrate, or the complex, in a fluid such as an aqueous or buffering medium. These are not the same; a suspension clearly includes the fluid in excess of the volume contained within the bounds of a particle. Thus Margel fails to provide the limitation recited in claims 7 and 16.

Margel does not remedy the deficiencies identified in Comb et al. with respect to independent claim 1 reciting the specificity-determiniing substrate of the invention, nor with respect to dependent claim 10 reciting the complex of the specificity-determining substrate with a protein. Specifically, no combination of Comb et al. with Margel provides the inventions, considered as a whole, provided in dependent claims 7 and 16. Accordingly Applicant submits that claims 7 and 16 are nonobvious under 35 U.S.C. 103(a) over the prior art of record. Applicant respectfully requests that this rejection be withdrawn at this time.

CONCLUSION

Applicant has shown that claims 1,2, 4-11, and 13-18, currently subject to examination under the species election provided by Applicant, are patentable over all grounds of rejection presented in the Office Action. Applicant respectfully requests that these rejections be withdrawn at this time.

Upon finding that claims 1,2, 4-11, and 13-18 as currently restricted are patentable, Applicant respectfully requests that all of claims 1-18 be examined with respect to all species therein.

Respectfully submitted,

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